Streptococcal Toxic Shock Syndrome From a Puncture Wound to the Foot

Puncture wounds to the foot are a common occurrence. If treated properly, the majority will be resolved without major complications. Toxic shock syndrome and streptococcal toxic shock-like syndrome are devastating complications of some staphylococcal and streptococcal infections. This paper discusses the similarities and differences between the two toxic states, reviews the pathophysiology, and presents a case report of near-fatal streptococcal toxic shock-like syndrome secondary to a puncture wound of the foot. (The Journal of Foot and Ankle Surgery 35(6):578–584, 1996)

Key words: toxic shock syndrome, streptococcal toxic shock syndrome, puncture wound

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During the past several years, group A streptococci have gained significant media attention. In May 1990, Jim Henson of the "Muppets" died from pneumonia caused by an unusually aggressive group A *streptococcus* (1). The media and medical journals have correctly reported the resurgence of group A streptococcal infections. Increases in rheumatic fever, group A streptococcal bacteremias, and the description of streptococcal toxic shock-like syndrome have been reported. These have occurred despite the continued availability of effective antibiotics and proper wound care, and, therefore, must be attributed to the changing virulence of streptococcal infections (2). There has, in fact, been a reappearance and resurgence of exotoxin-producing strains of streptococci, considered to be the etiologic agent responsible for streptococcal toxic shock-like syndrome.

The similarities to staphylococcal toxic shock syndrome are many, allowing many of the same principles learned from these toxic shock cases to be used in the newly encountered strep toxic shock cases. Toxic shock syndrome was first described in 1978 (3). Reports of similar syndromes can be found as far back as 1927 (2, 3), although they were not recognized as such at that time. Toxic shock syndrome became more frequently recognized in the early 1980s, when large numbers of cases were reported among young menstruating women (4), thereby generating a great deal of media publicity. The mortality rate of staphylococcal toxic shock syndrome is approximately 3% (2). Phage group I *Staphylococcus aureus* has been named the responsible pathogen in toxic shock syndrome. This strain of *Staphylococcus* produces an exotoxin known as toxic shock syndrome toxin 1 (TSST-1). There are currently six staphylococcal toxins that belong to a family known as superantigens. These toxin-producing strains are also a major cause of food poisoning (5).

Streptococcal toxic shock syndrome was first described by Cone *et al.* (6) in 1987, although a mention of this syndrome was suggested by Willoughby and Greenberg (7) in 1983. This new syndrome was given the name streptococcal toxic shock-like syndrome or toxic streptococcal syndrome (6, 8). Stevens, Tanner, and Winship (9), in 1989, reported 20 patients with streptococcal toxic shock-like syndrome with a case fatality rate of 30%, fully 10 times the mortality rate of its staphylococcal relative. This streptococcal syndrome is caused by group A β-hemolytic streptococci or *Streptococcus pyogenes.* Group A streptococci are responsible for the production of a variety of extracellular substances, including the cytotoxins and the hemolysins, streptolysin O and S, as well as streptokinase. Exotoxins produced by the streptococcus bacteria are categorized as types A, B, and C (2). These exotoxins function as superantigens, similar to TSST-1 of *Staphylococcus.* Exotoxin type A is most frequently reported, but combinations of the three types have been seen as well (2). These substances elaborated by the group A streptococci are powerful physiologic

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The Journal of Foot and Ankle Surgery 1067-2516/96/3506-0578$3.00/0

toxins, and, as a result, the streptococcal toxic shock like-syndrome is frequently fatal, with the course and sequellae being worse than that seen in toxic shock syndrome produced by *Staphylococcus* (2, 9, 10).

Clinical Features

Typical features of streptococcal and staphylococcal toxic shock syndrome are expressed in Tables 1 and 2. Group A *Streptococcus* and *Staphylococcus aureus* are responsible for a wide variety of otherwise nonfatal clinical illness and are virtually ubiquitous in the human bacteriologic environment. These illnesses range from mild skin infections (impetigo, pyoderma, and cellulitus) to pharyngitis, pneumonia, and septicemia. Streptococcal toxic shock-like syndrome and staphylococcal toxic shock syndrome, conversely, have been reported to ensue from various types of staphylococcal and streptococcal infections, including empyema, septic abortion, necrotizing fasciitis, osteomyelitis, abscess, mucous membrane colonization, surgical sites, and trauma (5, 11–18).

Patients afflicted with both syndromes typically describe a prodromal influenza-like illness with fever, chills, myalgias, diarrhea, and vomiting. The onset of symptoms is typically acute, with rapid progression over 48 to 72 hours (19). Extremity pain is often reported in streptococcal toxic shock-like syndrome, along with early local swelling and erythema (10). Skin, soft tissue, and mucus membrane findings can often hold early diagnostic clues for the onset of the syndromes. A diffuse macular erythroderma with late desquamation of the palms and soles is frequently seen in staphylococcal toxic shock syndrome, although less commonly in streptococcal toxic shock-like syndrome. Generalized nonpitting edema is often seen in staphylococcal toxic shock syndrome. Conjunctival and scleral hemorrhage, "strawberry tongue," and mucosal ulceration were frequently seen in staphylococcus and, less often, in streptococcal toxic shock-like syndrome. Bullae formation in streptococcal toxic shock-like syndrome was seen in 5 to 10% of cases, with necrotizing fasciitis or myositis in an amazing 70% of cases (10). Streptococcal myositis or fasciitis may also exist as a separate entity, but is most commonly seen as a component of the toxic shock-like state (20).

Blood cultures are positive approximately 50 to 58% of the time in streptococcal toxic shock-like syndrome (2, 10). In contrast, staphylococcal toxic shock syndrome has a much lower positive blood culture rate, reportedly

TABLE 1 Proposed case definition for streptococcal toxic shock syndrome

1. Isolation of group A streptococci
   - A. From a normally sterile site
   - B. From a nonsterile site
2. Clinical and laboratory signs
   - A. Hypotension: Systolic blood pressure ≤90 mm. Hg in adults or less than the fifth percentile for age in children
   - B. Two or more of the following
     1. Renal impairment: Creatinine ≥177 μmol./L. (≥2 mg./dL.) for adults or greater than or equal to twice the upper limit of normal for age. In patients with pre-existing renal disease, two-fold or greater elevation over baseline level.
     2. Coagulopathy: Platelets ≤(100,000/mm.^{3}) or disseminated intravascular coagulation defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products.
     3. Liver involvement: aspartate transaminase, alanine transaminase and/or total bilirubin levels greater than or equal to twice the upper limit of normal. In patients with pre-existing liver disease, two-fold or greater elevation over baseline.
     4. Adult respiratory distress syndrome defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure, or evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia.
     5. Generalized erythematous macular rash that may desquamate.
     6. General tissue necrosis, including necrotizing fasciitis or myositis, or gangrene.

Used with permission, from the Working Group on Severe Streptococcal Infections (8).

TABLE 2 Proposed case definition of toxic shock syndrome

1. Temperature ≥38.9°C (102°F)
2. Diffuse macular erythroderma or polymorphic maculopapular rash
3. Desquamation of the palms and soles 1 to 2 weeks after onset
4. Hypotension: Systolic blood pressure ≤90 mm. Hg in adults or less than the fifth percentile for age in children or orthostatic drop in systolic blood pressure ≥10 mm. Hg from lying to sitting position
5. Involvement of three or more of the following organ systems:
   - A. Gastrointestinal (vomiting or diarrhea at onset)
   - B. Muscular (severe myalgia or creatine phosphokinase level at least twice the upper limit)
   - C. Mucous membrane hyperemia (vaginal, oropharyngeal, or conjunctival)
   - D. Renal blood urea nitrogen or creatine at least twice the upper limit of normal or urinary sediment with pyuria (≥5 white blood cells per high power field) in the absence of a urinary tract infection
   - E. Hepatic (total bilirubin, aspartate transaminase, or alanine transaminase at least twice the upper limit)
   - F. Hematologic (platelets ≤100,000 per mm.^{3})
   - G. Central nervous system (disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent)
   - H. Absence of other bacterial, viral, or rickettsial infection, drug reaction, or autoimmune disorder

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between 10 and 15% (19, 10). Frequently, *S. aureus* can be locally cultured from clinically infected areas such as the super-absorbent tampons used during the early 80s. Nonmenstrual toxic shock syndrome usually has a positive culture from a suspected portal that recovers *S. aureus* (17). Seventy-five percent of patients with suspected staphylococcal toxic shock syndrome had positive isolates of TSST-1; the other 25% were found to produce other staphylococcal toxins (5). Conversely, streptococcal toxic shock-like syndrome produced exotoxins 90 to 95% of the time. Exotoxin type A was reported 29% of the time, type B 11%, and type C 0.06%. Various combinations of these toxins are found 53% of the time (2).

Other laboratory results are similar in both syndromes. Renal impairment is often seen as expressed by a serum urea nitrogen or creatinine at least twice the upper limit of normal. This is sometimes a secondary manifestation of profound hemodynamic instability or the tissue and muscle destruction associated with the toxins. Urinary sediment with pyuria in the absence of a urinary tract infection will usually be manifest. Hematological abnormalities are usually reported from disseminated intravascular coagulation (DIC): platelets < 100,000/mm, prolonged clotting times, low fibrinogen levels, and the presence of elevated fibrin degradation products (6, 19). DIC, in combination with vasopressors, which are frequently necessary to support central perfusion, often leads to the distal extremity severe vasoconstriction, micro- and macrocirculatory thrombosis, and consequent necrosis seen in the syndrome. Hepatic involvement shows levels of aspartate transaminase alanine transaminase, and/or total bilirubin two times the upper normal limit, probably from the same etiology. Severe leukocytosis with a shift to the left is common, as is manifestation of hypoalbuminemia and hypocalcemia in a smaller number of patients. In the acute stage, adult respiratory distress syndrome (ARDS) is sometimes seen in the more severe cases and is defined as diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure. In these patients, there is frequently evidence of diffuse capillary leak manifested by the acute onset of generalized edema, plural effusions, or peritoneal ascites with hypoalbuminemia (6, 19).

Streptococcal toxic shock-like syndrome is generally more devastating than staphylococcal toxic shock syndrome. Most patients present to the emergency room with a fever above 102°F. Hypotension and tachycardia seen in the hyperdynamic state of sepsis are common on presentation in both syndromes with a typical systolic blood pressure below 90 mm. Hg. Orthostatic dizziness and syncope are frequently observed secondarily to the vasodilatation-producing relative hypovolemia. Neurologic symptoms can be expected in both syndromes ranging from confusion to coma (19).

Late complications from these toxic syndromes, if not fatal, are often devastating. Stevens *et al.* (9) reported that 80% of their patients developed renal impairment, which was irreversible in 10%. Most survivors have had multiple surgical procedures consisting of fasciotomies, debridements, and amputations.

The differential diagnosis must include the exanthematous diseases: leptospirosis, Rocky Mountain spotted fever, scalded skin syndrome, rubeola, systemic lupus, and Kawasaki syndrome[5] (11). Other diseases with a similar clinical picture include Stevens-Johnson syndrome,[6] acute rheumatic fever, Legionnaires' disease, toxoplasmosis, and tic-borne typhus (21). Immediate differentiation from these other diseases must occur on presentation, since the toxic shock syndromes progress rapidly and inexorably once the cascade of toxins have had an opportunity to become established.

Case Report

A 35-year-old white male was brought to the emergency room by his wife, who stated he had complaints of vague stomach pains and increasing pain to his right foot in the last 24 hr. She related an incident that occurred 4 days previously, where he had punctured his right second toe while tiling his bathroom floor. She stated that she had applied a topical antibiotic to the area the night before because the area had become increasingly red. She also stated that her husband vomited and had diarrhea the morning of presentation.

Past medical history was significant in that the patient had a myelomeningocele repaired as a child with only moderate motor weakness and sensory loss to the lower extremity. He ambulated without assistance with a mildly noticeable limp. The patient is not on any other medication and has no history of drug allergies. He is a two-pack-a-day smoker and a social drinker. He had a tetanus booster 4 years earlier.

At presentation, his temperature was 102.6°F, pulse was 165/min, and respirations were 36/min. His blood pressure was 50/30 mm. Hg. Upon physical examination, the patient was obtunded and cyanotic. There was a diffuse erythematous rash from his face down to his feet that blanched with compression. The conjunctiva of his eyes and mucous membranes of his mouth were erythematous and injected. The right foot had an area of initial injury to the second toe, which appeared as a

[5] The clinical picture is almost identical to toxic shock syndrome, differential clues are cervical lymphadenopathy, lip erosions, increased platelets, and later coronary aneurysms secondary to arthritis.

[6] This is a hypersensitivity reaction with severe stomatitis with erosions developing symmetrically on acral surfaces, fever, headache, sore throat, rapid weak pulse, tachypenia, and arthralgia.

small laceration dorsally, about 1 cm. in length. The area was mildly erythematous without drainage, showing evidence of local cellulitis. The hands and left lower extremity were cool to the touch. Femoral pulses were palpable, but distal pulses could not be appreciated. The capillary refill was noted to be slow, but intact. There was no fluctuance or crepitance subcutaneously. His lungs were clear and his heart had a regular, but rapid rhythm. Abdominal and rectal examination were normal.

X-rays of the right lower extremity were negative and chest x-rays showed the beginning of adult respiratory distress syndrome. EKG showed a normal sinus rhythm. A noninvasive vascular examination showed Ankle Brachial Indices (ABIs) of 0.75 on the right and 0.7 on the left. Doppler testing was biphasic at all levels except the left dorsalis pedis.

His laboratory data were notable for a white blood cell count of 13,500/mm. 3 (normal 4800 to 10,800/mm. 3) with a differential of 78% segmented forms (normal 50 to 70%), 11% band forms (normal 0 to 5%), 4% lymphocytes (normal 20 to 40%), 4% monocytes (normal 0 to 12%), 1% metamylocytes (normal 0%). His electrolyte laboratory revealed the following levels: sodium, 135 mEq./L. (normal 135 to 150 mEq./L.); potassium, 3.2 mEq./L. (normal 3.5 to 5.0 mEq./L.); chloride, 111 mEq./L. (normal 100 to 110 mEq./L.); bicarbonate, 11 mEq./L. (normal 25 to 32 mEq./L.); calcium, 6.5 mg./dL. (normal 8.5 to 10.5 mg./dL.); phosphorus, 7.0 mg./dL. (normal 2.7 to 4.5); blood urea nitrogen, 52 mg./dL. (normal, 8 to 22 mg./dL.); creatinine, 4.9 mg./dL. (normal, 0.8 to 1.6 mg./dL.); and blood sugar, 78 mg./dL. (normal 70 to 115 mg./dL.). His prothrombin time was 12.8 sec. (normal 10.7 to 13.6), and the partial thromboplastin time was 46 sec. (normal 20 to 36 sec.). The fibrinogen level was 391 mg./dL. (normal, 200 to 400 mg./dL.), and the fibrin degradation product level was >40 mg./L. (normal, <10 mg./L.). Platelets were 35 k/mm.^{3} (normal, 150 to 400 k/mm.^{3}).

His liver function test was notable, since it revealed the following levels: lactate dehydrogenase, 1330 units/L. (normal 110 to 200 units/L.); alkaline phosphate, 81 units/L. (normal, 35 to 180 units/L.); bilirubin, 2.0 mg./dL. (normal, 0 to 1.5 mg./dL.); total protein, 4.5 gm./dL. (5.5 to 8.0 gm./dL.); albumin, 2.8 gm./dL. (normal, 3.0 to 5.0 gm./dL.); globulin, 1.7 gm./dL. (normal, 2.5 to 4.0 gm./dL.); aspartate transaminase 197 units/L. (normal, 0 to 37 units/L.); alanine transaminase 71 units/L. (normal, 110 to 200 units/L.); creatine kinase, 4735 units/L. (normal, 20 to 150 units/L.); and CK-MB, 10.2 ng./mL. (normal, 0 to 5 ng./mL.). The index was 0.2 (normal, 0 to 2.5).

An arterial blood gas examination during administration of 100% oxygen by mask revealed a pH of 7.26 (normal, 7.35 to 7.45), a P_{CO_2} level of 26 mm. Hg (normal, 32 to 43 mm. Hg), a P_{CO_2} level of 109 mm. Hg (normal, 83 to 108 mm. Hg), and an oxygen saturation level of 85% (normal, 95 to 99%). Urinalysis showed many tubular cells and epithelial cells, along with white blood cells and bacteria. Wound cultures of the right foot wound produced *Staphylococcus epidermidis* and group A streptococci, stool and respiratory cultures produced yeast, and blood cultures found group A streptococci. A toxin screen on the *Streptococcus* strain showed the production of exotoxin A and exotoxin B.

The patient was admitted to the intensive care unit and started on rapid hydration, penicillin G, and ceftriaxone™.[7] He was placed on levophed™[8] and dopamine[9] which held his blood pressure around 104/80 mm. Hg. On day two, the patient continued to become acidotic with progression of his ARDS and the acral cyanosis became increasingly evident. Multiple areas of fluid-filled bullae were noted on the lower extremity, along with loss of capillary refill to the distal extremities. At this time, the patient was intubated and placed on a Swan-Ganz catheter.[10]

Multiple medical disciplines were consulted throughout the stay concerning the care of this patient. His condition slowly stabilized over the next 18 days. He was extubated on the sixth day, and his liver and kidney function also stabilized. At this time, the distal ischemic process had declared itself—dry gangrene was noted in the digits of both hands (Fig. 1); the tip of the nose, ear lobes, and penis; the distal right foot (Fig. 2); and the entire left foot (Fig. 3). Over the next 8 weeks, the patient had multiple surgical procedures. The hands were amputated at the proximal phalanx bilaterally. The right foot had a transmetatarsal amputation, and also required a split-thickness skin graft to the dorsal lateral foot and to the medial malleolar area (Fig. 4). The left foot was guillotine-amputated to prevent progression of infection at 4 weeks. The left leg then required a below-knee amputation (Fig. 5). Other areas of bulla formation healed uneventfully over the 8-week course. The patient is currently 14 months from initial injury. He went through extensive occupational and physical therapy, and currently is able to ambulate with assistance using a walker and a left leg prosthetic. His liver and kidney function eventually returned to pre-injury levels.

Discussion

Streptococcal toxic shock-like syndrome occurs in all age groups, although it is most commonly encountered between the ages of 20 and 50. Children >5 years of age have been reported to have a greater chance of survival

[7] Hoffman-Laroche, Inc., 340 Kingsland St., Nutley, NJ 07110.
[8] Sanofi-Winthrop, 90 Park Ave., New York, NY 10016.
[9] Elkins-Sinn, Inc., 2 Esterbrook Lane, Cherryhill, NJ 08003.
[10] Arrow International, 300 Burnville Road, Reading, PA 19605.

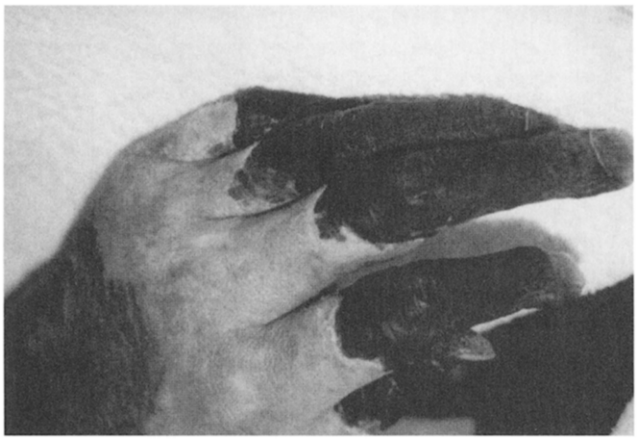

FIGURE 1 Left hand showing distal mummification of digits.

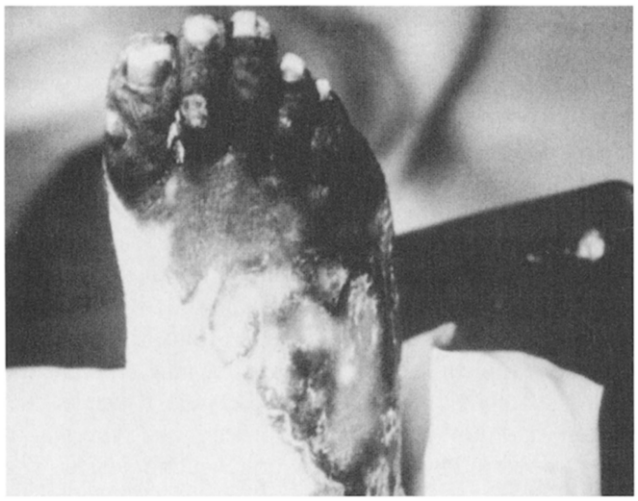

FIGURE 2 Right foot showing progression of ischemia. Note the second digit, where injury occurred.

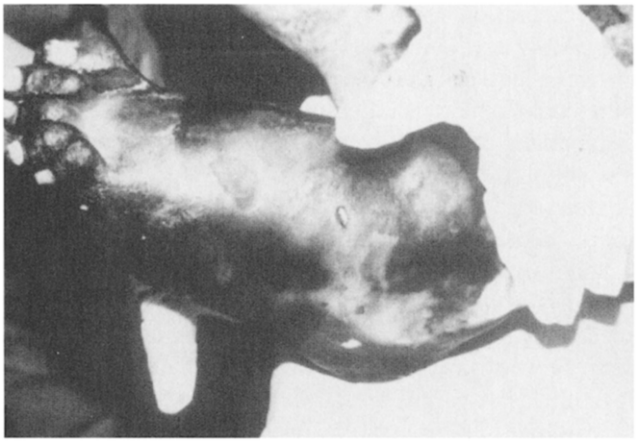

FIGURE 3 Left foot dry gangrene of entire foot.

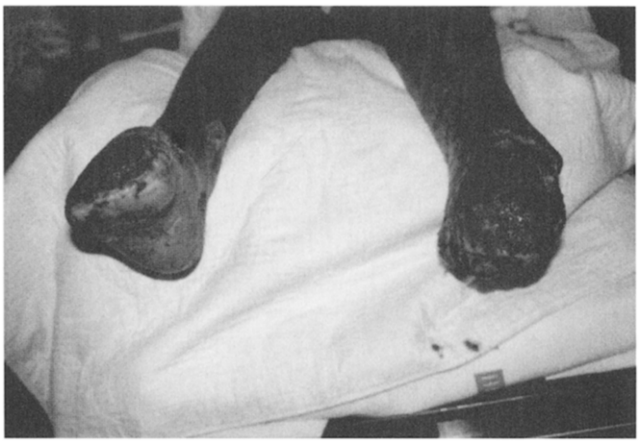

FIGURE 4 Appearance of lower extremities following first debridement.

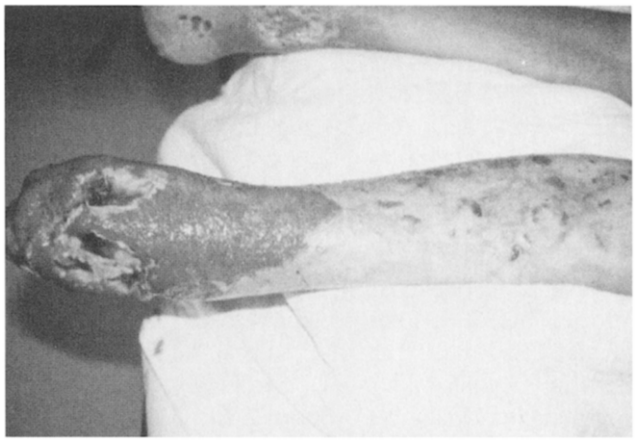

FIGURE 5 Preoperative left leg for below-knee amputation.

after streptococcal toxic shock-like syndrome (22). The incidence in adults has been reported to be from 2.6 to 4.3 per 100,000 population (22, 23). Interestingly, the incidence of staphylococcal toxic shock syndrome during the peak of the early 1980s epidemic was 8 to 14 per 100,000 (21), whereas today, the incidence is closer to between 1 and 2 per 100,000. Women aged 15 through 44 years are at a higher risk due to menstruation, as are whites, who account for 80% of the nonmenstrual cases reported (21). In the postoperative setting, the threat exists, although it is extremely low. A 12-year retrospective review studied 390,000 surgical procedures and found an incidence of staphylococcal toxic shock syndrome to be only 0.003% (12 cases) (13).

A comprehensive understanding of the pathophysiology of sepsis has not yet been elucidated. However, it is believed that a complex mechanism involving activation of many different cellular species occurs, most notably among the monocytes, T-cells, neutrophils, and platelets. Cytokines, such as tumor necrosis factor and other interleukins, are released. The arachidonic cascade is thus triggered and complement and coagulation systems are subsequently activated, resulting in widespread endothelial inflammation and dramatically increased capillary permeability. This

process proceeds at an alarming rate and, unless rapidly interrupted, presents as shock (5, 24).

Since this is a toxin-mediated disease, a basic review of the steps in the toxic cascade will be useful in understanding the destructive process of this syndrome. Staphylococcal enterotoxins TSST-1 and streptococcal exotoxins A, B, and C are also known as superantigens. These have been reported to be the greatest stimulators of T-cells known. Superantigens exhibit two contradictory effects; in the early stage, they cause a proliferation of T-cells, then later T-cell death occurs. This increase stimulates the release of tumor necrosis factor, interleukins, and other cytokines. These products, in the correct amount, are beneficial, but the cascade runs out of control and loses its ability to regulate itself. Toxins also increase membrane permeability, especially to calcium ions. This, in turn, creates gaps in the endothelial layer, permitting free passage of molecules (24, 25), resulting in interstitial edema, loss of serum osmotic pressure, and intravascular depletion.

Tests on the toxins of scarlet fever and TSST-1 have shown that they can cause profound fever and shock. Exotoxin A, as is found in streptococcal toxic shock-like syndrome, has been shown to be much more potent than TSST-1 in its ability to produce fever, cachexia, multiple organ dysfunction, and death. TSST-1 can also have detrimental effects on myocardial function, not only producing myocardial edema, but also incorporating a direct myocardial depressant factor. Other examples of superantigens reported in the literature include the exoprotein of mycoplasma arthritidies, *Clostridium perfringes* enterotoxin, a toxin from *Yersinia enterocolitica,* and the nucleocapsid of the rabies virus (24).

The presence of toxin-producing strains of *Streptococcus* and *Staphylococcus* is clearly necessary to produce the fulminant course of the disease. Numerous studies have demonstrated that nasal and vaginal colonization of *S. aureus* that produce TSST-1 is quite common. Why then is toxic shock syndrome itself so rare? The answer may lie in the presence of pre-existing antibodies to these toxins. By the age of 20 to 25 years, 90% of the population will have developed anti-TSST-1 antibodies. This antibody has been shown to provide protection against the syndrome (4).

Treatment

The invasive nature of these serious infections requires prompt diagnosis and treatment. The strict case definition specific by the Working Group on Severe Streptococcal Infections emphasizes the occurrence of shock and multiorgan failure early in the course of the infection (6). This clinical representation must be combined with collection of appropriate cultures from focal infections, Gram stain and culture, blood or skin biopsy, laboratory results, and a clinical picture to obtain a correct diagnosis. It cannot be emphasized enough, however, that early diagnosis and rapid initial treatment are critical in the prognosis of the disease. Waiting until shock and multi-organ failure supervene invite high mortality. Streptococcal and staphylococcal toxic shock patients need intensive fluid replacement, pressor support, and intravenous antibiotics. Many patients are admitted to the intensive care unit and subsequently require mechanical ventilation and hemodialysis. Early surgical intervention may be required to drain abscesses, or halt progressive necrotizing fasciitis or myositis with radical debridement. Late surgical reconstruction, including skin grafts, amputations, and muscle and/or skin free flaps may become necessary. Proper consultation should address internal medicine, general surgery, vascular surgery, plastic surgery, infectious diseases, medicine, physical therapy, psychiatry, social work, and prosthetics.

Penicillin G is recommended for group A *Streptococcus* treatment as well as prevention, and has been so for nearly 50 years (10). Reports of failures of penicillin G have occurred, however, and this may prove to have serious consequences. Eagle *et al.* (27) claimed that penicillin was ineffective in eradicating *Streptococcus* from tissues if the organism were present in high enough concentrations. During the "Eagle effect," the slow rate of replication of the bacteria halts the turnover of penicillin-binding proteins, thus decreasing the antimicrobial effect of penicillin (10, 26, 27). Although there is no documentation yet, the addition of clindamycin™, a protein synthesis inhibitor, may have a theoretical advantage (2). In the penicillin-allergic patient, either clindamycin or erythromycin™ is a good choice, but reports of resistance even to these antibiotics has been noted (10). Antibiotic treatment should cover a broad spectrum until appropriate cultures have been obtained. In the case of staphylococcal toxic shock syndrome, a β-lactamase-resistant antistaphylococcal antibiotic such as oxacillin™[11] or nafcillin™[12] should be administered.

Unfortunately, antibiotics have no effect on toxin loads, and it is the toxin that produces most of the tissue damage, and provides an environment that allows bacterial replication. Recently, new advances have been made and may soon be available (24, 28). Two of the most promising new treatments are an antagonist to interleukin-1, and monoclonal antibodies to tumor necrosis factor, both of which have been shown to slow the inflammatory cascade in animal models. Another agent that may slow the inflammatory cascade includes pentoxifylline™,[13] which inhibits neutrophils and decreases the tendency of blood to clot.

[11] Biocraft Lab, Inc., 1801 Rillen Road, Fairlawn, NJ 07410.
[12] Wyeth-Ayerst Labs, P.O. Box 8299, Philadelphia, PA 19101.
[13] Hoechst-Roussel Pharmaceuticals, Route 202–206, P.O. Box 25 Sommerville, NJ 08876.

Cyclo-oxygenase and thromboxane synthetase inhibitors have also been shown to be effective. Antitoxins have been developed, but the drawback is that they are specific to a single class of organisms (28, 29). Of course, none of these agents will ever replace proper antibiotics, drainage, and debridement of infected tissues. The future holds much promise for better treatment of toxic-mediated diseases, due to ongoing research, combined with far better understanding of the pathophysiology of the disease process.

Conclusion

Streptococcal and staphylococcal toxic shock syndrome are devastating diseases for any patient to have, and any physician to treat. Since many traumatic injuries to the feet provide portals of entry for these virulent organisms, podiatric physicians must be aware of the presenting symptoms of these syndromes. In patients presenting in any clinical setting with fever, hypotension, rash, and/or multi-organ failure, a toxic shock syndrome must be suspected. Timely diagnosis and treatment must be initiated, along with proper referrals. Although the incidence of these syndromes is, fortunately, fairly low, they must always be kept high on a differential list. It is only by early diagnosis and aggressive treatment that we may prevent the devastating complications of toxic shock syndromes.

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